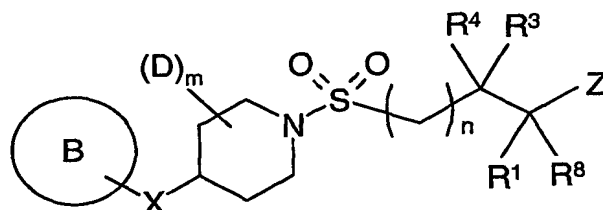


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CLAIMS:

What we claim is :-

1. A compound of formula (1):



formula (1)

Z is selected from $-\text{CONR}^{15}\text{OH}$ and $-\text{N}(\text{OH})\text{CHO}$;

R^{15} is hydrogen or C_{1-3} alkyl;

R^1 is hydrogen or a group selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{5-7} cycloalkenyl, aryl and heteroaryl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl (optionally substituted by one or more R^{17}), aryl (optionally substituted by one or more R^{17}), heteroaryl (optionally substituted by one or more R^{17}), heterocyclyl, C_{1-4} alkoxycarbonyl, $-\text{OR}^5$, $-\text{SR}^2$, $-\text{SOR}^2$, $-\text{SO}_2\text{R}^2$, $-\text{COR}^2$, $-\text{CO}_2\text{R}^5$, $-\text{CONR}^5\text{R}^6$, $-\text{NR}^{16}\text{COR}^5$, $-\text{SO}_2\text{NR}^5\text{R}^6$ and $-\text{NR}^{16}\text{SO}_2\text{R}^2$;

R^{16} is hydrogen or C_{1-3} alkyl;

R^{17} is selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl and C_{1-6} alkoxy;

R^2 is group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is optionally substituted by one or more halo;

R^5 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is optionally substituted by one or more halo;

R^6 is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;

or R^5 and R^6 together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

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R^8 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-7} cycloalkyl and C_{5-7} cycloalkenyl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and C_{1-4} alkyl;

R^3 and R^4 are both hydrogen;

5 n is 0 or 1;

m is 0 or 1;

D is hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl or fluoro;

X is $-(CR^9R^{10})_t-Q-(CR^{11}R^{12})_u-$ where t and u are independently 0 or 1 with the proviso that t and u cannot both be 0;

10 Q is O, S, SO or SO_2 ;

R^9 , R^{10} , R^{11} and R^{12} are independently selected from hydrogen, C_{1-4} alkyl and C_{3-6} cycloalkyl;

B is a group selected from aryl, heteroaryl, heterocyclyl, C_{3-10} cycloalkyl and C_{5-7} cycloalkenyl where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C_{1-4} alkyl (optionally substituted by one or

15 more R^{13}), C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl (optionally substituted by one or more R^{13}), heterocycloalkyl, heteroaryl, aryl, $-OR^{13}$, cyano, $-NR^{13}R^{14}$, $-CONR^{13}R^{14}$, $-NR^{16}COR^{13}$, $-SO_2NR^{13}R^{14}$, $-NR^{16}SO_2R^{13}$, $-SR^{13}$, $-SOR^7$ and $-SO_2R^7$;

R^7 is C_{1-6} alkyl or C_{3-6} cycloalkyl

R^{13} and R^{14} are independently hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;

20 or R^{13} and R^{14} together with the nitrogen to which they are attached form a heterocyclic 4 to 7-membered ring.

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

2. A compound according to claim 1 wherein X is $-(CH_2)-O-$, $-O-(CH_2)-$, $-(CH_2)-O-$
25 $(CH_2)-$ or $-(CHMe)-O-$.

3. A compound according to claim 1 or 2 wherein R^1 is C_{1-4} alkyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, aryl, heteroaryl and C_{1-4} alkyl substituted by aryl or heteroaryl wherein any R^1 group is optionally substituted by one or more substituents independently selected from halo,
30 cyano, nitro, C_{1-4} alkoxy, C_{1-4} alkyl, trifluoromethyl and trifluoromethoxy.

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4. A compound according to any one of claims 1 to 3 wherein B is a group selected from aryl, heteroaryl, heterocyclyl, C₃₋₁₀cycloalkyl and C₅₋₇cycloalkenyl where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, halo, C₁₋₄alkyl, heteroaryl, -OR¹³, cyano, -NR¹³R¹⁴, -CONR¹³R¹⁴ and -NR¹⁶COR¹³.
5. A compound according to claim 4 wherein B is aryl, heteroaryl or C₃₋₆cycloalkyl optionally substituted by 1, 2 or 3 groups independently selected from C₁₋₄alkyl, halo, cyano, nitro, C₁₋₄alkoxy and trifluoromethyl
6. A compound according claim 5 wherein B is 2,5-dimethylphenyl or 2-methylquinolin-4-yl.
7. A compound according to claim 1, selected from:
- (R/S)-1-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl)sulphonyl)methyl]-4-pyrimidin-2-ylbutyl(hydroxy)formamide;
- (R/S)-1-methyl-2-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl)sulphonyl]ethyl(hydroxy)formamide;
- (R/S)-1-pyrid-3-yl-2-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl)sulphonyl]ethyl(hydroxy)formamide;
- (R/S)-1-(1H-imidazol-4-yl)-2-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl)sulphonyl]ethyl(hydroxy)formamide;
- (R/S)-2-[(4-[(2,5-dimethylbenzyl)oxy]piperidin-1-yl)sulphonyl]-1-pyrid-3-ylethyl(hydroxy)formamide;
- (R/S)-[1-[(4-(2,5-dimethylbenzyloxy)piperidin-1-yl)sulphonyl]methyl]-3-phenylpropyl]hydroxyformamide;
- (R/S)-2-[(4-[(2,5-dimethylbenzyl)oxy]piperidin-1-yl)sulphonyl]-1-[4-fluoro-2-(trifluoromethyl)phenyl]ethyl(hydroxy)formamide;
- (R/S)-2-[(4-[(2,5-dimethylbenzyl)oxy]piperidin-1-yl)sulphonyl]-1-[2-(trifluoromethyl)phenyl]ethyl(hydroxy)formamide;
- (R/S)-2-[(4-[(2,5-dimethylbenzyl)oxy]piperidin-1-yl)sulphonyl]-1-[3-(trifluoromethyl)phenyl]ethyl(hydroxy)formamide;

- (R/S)-2-({4-[(2,5-dimethylphenoxy)methyl]piperidin-1-yl}sulphonyl)-1-(4-fluorophenyl)ethyl(hydroxy)formamide;
- (R/S)-1-{{4-[(2,5-dimethylbenzyl)oxy]methyl}piperidin-1-yl}sulphonyl)methyl}-4-pyrimidin-2-ylbutyl(hydroxy)formamide
- 5 (R/S)-2-methyl-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propionic hydroxamic acid
- (R/S)-2-({4-[(2,5-difluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide
- (R/S)-hydroxy(1-phenyl-2-{[4-(pyridin-2-ylmethoxy)piperidin-1-yl]sulphonyl}ethyl)formamide;
- 10 (R/S)-hydroxy(1-phenyl-2-{[4-(pyridin-3-ylmethoxy)piperidin-1-yl]sulphonyl}ethyl)formamide;
- (R/S)-2-({4-[(2,6-difluoro-3-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- 15 (R/S)-2-({4-[(2-chloro-6-fluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(5-fluoro-2-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-{[4-(benzyloxy)piperidin-1-yl]sulphonyl}-1-phenylethyl(hydroxy)formamide;
- 20 (R/S)-hydroxy[2-({4-[(2-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl]formamide;
- (R/S)-2-({4-[(3-chlorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(2-bromobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- 25 (R/S)-2-({4-[(2-fluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(2,6-difluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- 30 (R/S)-2-({4-[(3-fluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;

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- (R/S)-hydroxy{1-phenyl-2-[(4-{[4-(trifluoromethyl)benzyl]oxy}piperidin-1-yl)sulphonyl]ethyl}formamide;
- (R/S)-2-{[4-(cyclohexylmethoxy)piperidin-1-yl]sulphonyl}-1-phenylethyl(hydroxy)formamide;
- 5 (R/S)-2-({4-[(4-bromobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(4-fluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(2,5-dimethylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- 10 (R/S)-2-({4-[(2-fluoro-3-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-phenylethyl(hydroxy)formamide;
- (R/S)-hydroxy[2-({4-[(2-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;
- 15 (R/S)-hydroxy[2-({4-[(4-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;
- (R/S)-2-({4-[(2-fluorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(2-chlorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;
- 20 (R/S)-2-({4-[(2,4-dichlorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;
- (R/S)-2-({4-[(2,6-dichlorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;
- 25 (R/S)-hydroxy[2-({4-[(mesitylmethoxy)piperidin-1-yl]sulphonyl)-1-pyridin-3-ylethyl]formamide;
- (R/S)-2-({4-[(3,4-dichlorobenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;
- (R/S)-hydroxy[2-({4-[(3-methoxybenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;
- 30 (R/S)-hydroxy[2-({4-[(3-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;

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(R/S)-2-({4-[(3,4-dimethylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;

(R/S)-hydroxy[2-({4-[(4-methoxybenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;

5 (R/S)-hydroxy[2-({4-[(4-isopropylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl]formamide;

(R/S)-2-({4-[(3-chloro-4-methylbenzyl)oxy]piperidin-1-yl}sulphonyl)-1-pyridin-3-ylethyl(hydroxy)formamide;

(R/S)-N-hydroxy-N-isopropyl-2-methyl-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propanamide;

hydroxy{(1R)-1-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)methyl]-4-pyrimidin-2-ylbutyl}formamide;

hydroxy{(1S)-1-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)methyl]-4-pyrimidin-2-ylbutyl}formamide;

15 (2R)-N-hydroxy-2-methyl-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propanamide

(R/S)-2-cyclopentyl-N-hydroxy-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propanamide;

(2S)-2-cyclopentyl-N-hydroxy-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propanamide;

(2R)-2-cyclopentyl-N-hydroxy-3-({4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)propanamide;

(2S)-N-hydroxy-4-methyl-2-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)methyl]pentanamide;

25 (2R)-N-hydroxy-4-methyl-2-[(4-[(2-methylquinolin-4-yl)methoxy]piperidin-1-yl}sulphonyl)methyl]pentanamide; and

(R/S)-N-{1-[4-(2,6-dimethyl-pyridin-4-ylmethoxy)-piperidine-1-sulphonylmethyl]-4-pyrimidin-2-yl-butyl}-N-(hydroxy)formamide.

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8. A compound according to claim 1 for use as a medicament.

9. The use of a compound according to claim 1 in the manufacture of a medicament in the treatment of a disease condition mediated by one or more metalloproteinase enzymes.

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10. The use of a compound according to claim 1 in the manufacture of a medicament in the treatment of a disease condition mediated TNF α .

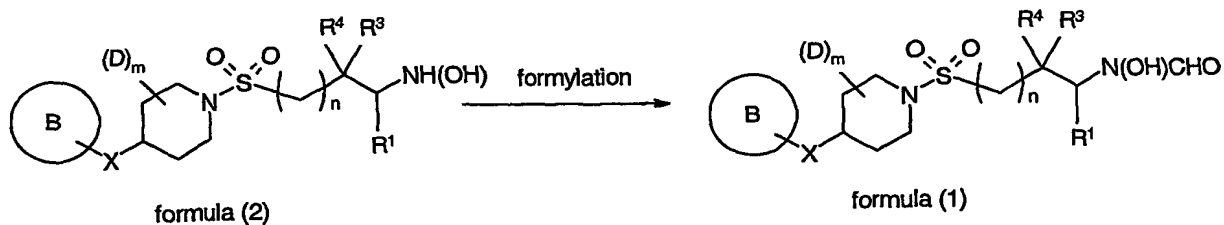
11. A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound according to claim 1.

12. A pharmaceutical composition comprising a compound according to claim 1; and a pharmaceutically-acceptable diluent or carrier.

13. A process for preparing a compound according to claim 1 which comprises; when Z is -N(OH)CHO, the step of:

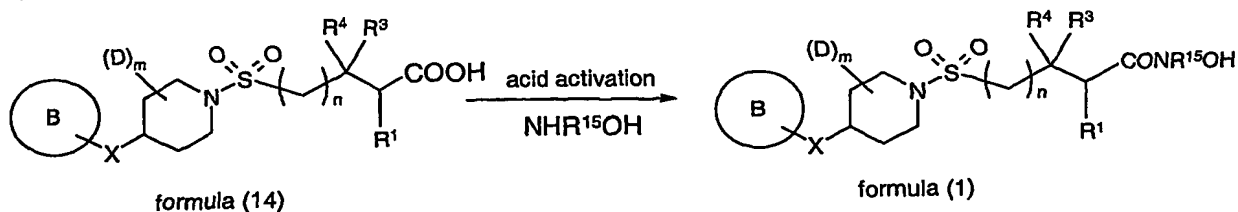
a) converting a hydroxylamine of formula (2) into a compound of formula (1);

20



or where Z is -CONR¹⁵OH the step of;

b) converting an acid of formula (14) into a compound of formula (1);



25 and thereafter if necessary:

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- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.